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酰胺的直接转化: 仲酰胺与丹尼谢夫斯基双烯的还原环加成反应

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摘要 酰胺作为稳定的合成中间体被广泛应用于有机合成和药物化学. 因此, 发展通用、化学选择性的酰胺直接转化的方法十分重要. 在本工作中, 我们报道仲酰胺与丹尼谢夫斯基双烯的还原环加成反应, 用于把仲酰胺直接转化为 2-取代-2,3-二氢-4-吡啶酮. 该"一瓶反应"包含酰胺通过三氟甲磺酸酐活化、部分还原、和[4+2]环加成反应 3 个环节. 基于这一步骤经济型方法, 建立了生物碱(±)-lasubine I 和(±)-myrtine 的简便、无保护基全合成.

关键词 酰胺; 一瓶反应; 环加成反应; 活化; 三氟甲磺酸酐; 生物碱

Direct Transformation of Amides: Reductive Cycloaddition of Secondary Amides with Danishefsky Diene

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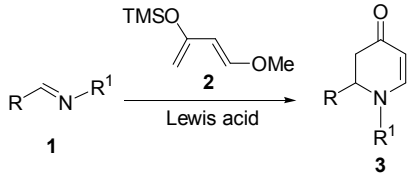
Abstract Amides are widely used as stable synthetic intermediates in organic synthesis and medicinal chemistry. Versatile and chemoselective C—C bond forming methods for the direct transformation of amides are highly demanding. In this paper, we report the reductive cycloaddition of common secondary amides with the Danishefsky diene to produce 2-substituted 2,3-dihydro-4-pyridones. This one-pot procedure involves amide activation with triflic anhydride, partial reduction, and [4+2] cycloaddition. The synthetic utility of this step-econimical method was demonstrated by the short and protecting-group-free total syntheses of alkaloids (±)-lasubine I and (±)-myrtine.

Keywords amides; one-pot reaction; cycloaddition reaction; activation; triflic anhydride; alkaloids

1 Introduction

Amides are commonly used as advantageous synthetic intermediates in organic synthesis and medicinal chemistry because of their high stability.[1,2] When employed as synthetic intermediates, the amide group needs to be converted into other needed functional group at a latter stage of a synthetic sequence. In recent years, significant progress has been made in the one-pot transformation of amides into other classes of compounds via C—C bond formation reactions.[3] Notable examples include the reductive cyanation of secondary amides,[4] the Vilsmeier-Haack-type cyclizations/reactions,[5] the reductive bisalkylation of tertiary amides,[6] the reductive cyclization of secondary amide,[1h,1l] reductive alkylation/functionalization of secondary[7] and tertiary[8] amides, reductive alkylation/functionalization of *N*-alkoxylamides,[9,3b] deaminative alkylation of secondary amides,[10] the amide-based Claisen rearrangement,[11] the nitro-Mannich reaction,[12] tertiary amides-based knoevenagel-type reactions,[13] and reductive coupling of secondary amides.[14]

The [4+2] cycloaddition using an imine as the dienophile has been known for over seventy years.[15] The seminal work of Danishefsky has paved the Lewis acid-promoted [4+2] aza-cycloaddition of imines **1** with electon-riched silyloxydienes such as 1-methoxy-3- trimethylsilyloxy-1,3-butadiene (the Danishefsky diene **2**, Scheme 1).[16] This reaction has become a powerful tool for the construction of 2,3-dihydro-4-pyridone derivatives **3**.[17] The versatility of **3** for the synthesis of piperidine-



Scheme 1 The Lewis acid-promoted aza-cycloaddition of Danishefsky diene with aldimines

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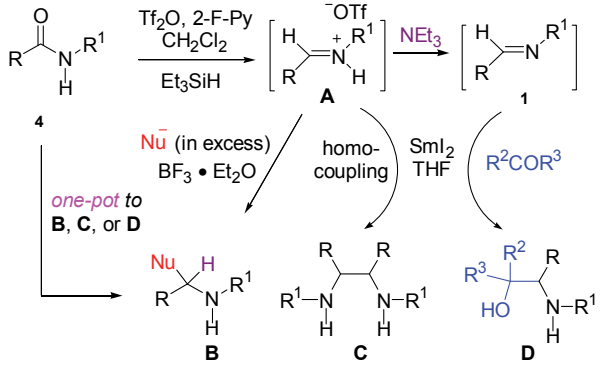
containing alkaloids has been demonstrated.[18]

Although significant progress has been achieved recently on novel C—C bond forming reactions from amides,[3~14] to the best of our knowledge there is no report on the use of common secondary amides for the one-pot synthesis of 2-substituted 2,3-dihydro-4-pyridones. As part of our program to develop efficient methods for the synthesis of *N*-containing molecules,[19] we have been interested in developing C—C bond forming reactions starting from common amides [7e,7f,8b~8d,8f,10b,10c,13,14] based on the *in situ* amide activation with triflic anhydride (Tf_2O).[20] Continuing the effort, we report herein the one-pot reductive cycloaddition of secondary amides **4**[21] with the Danishefsky diene **2** for the synthesis of 2,3-dihydro-4-pyridones and its application in the total syntheses of quinolizidine alkaloids (±)-lasubine I (**5**) and (±)-myrtine (**6**).

We reported recently that the iminium ion **A** generated *in situ* from a secondary amide **4** by successive treatment with Tf_2O/2-F-Py (2-fluoropyridine) and triethylsilane[22] can participate in several C—C bond forming reactions to afford functionalized amines **B**,[7f] vicinal diamines **C**,[14] or *β*-amino alcohols **D**[14] (Scheme 2). We envisioned that under appropriate conditions, the imines **1** may also be captured by the Danishefsky diene **2** to give 2,3-dihydro-4-pyridones **3** (cf. Scheme 1).

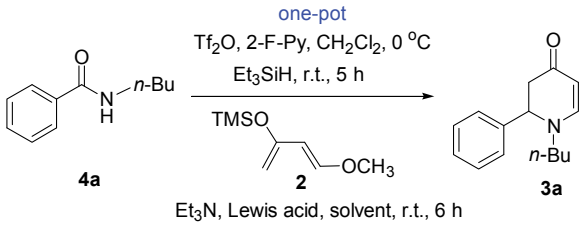


Scheme 2 C—C Bond forming reactions of the iminium ions generated *in situ* from secondary amides

2 Results and Discussion

N-Butylbenzamide **4a** was chosen as the model substrate for our investigation. Thus **4a** was treated sequentially with Tf_2O (1.1 equiv.) and 2-F-Py (1.2 equiv.) at 0 ℃ for 30 min, Et_3SiH at 0 ℃ to r.t. for 5 h, the Danishefsky diene, triethylamine (2 equiv.) and a Lewis acid (1.5 equiv.) at r.t. for 6 h (Table 1). To our delight, the use of Lewis acids like $ZnCl_2$, BF_3•Et_2O, TMSOTf and $TiCl_4$, did lead to the formation of the desired product **3a** in 59%, 39%, 35% and 22% yield, respectively (Table 1, Entries 1~4). In 2002, Ding reported that the aza-Diels-Alder reaction benefits from the use of polar solvents.[17f] Inspired by this work, we screened different solvents for the cycloaddition step and were pleased to find that the yield was improved to 80% in MeOH.[17f] Other solvents such as THF and MeCN were less effective. In comparison, the use of non-polar solvents such as diethyl ether and toluene led to only trace or no desired adduct (Table 1, Entries 7 and 8). Thus, the optimal conditions for the one-pot reduction of secondary amides and tandem cycloaddition of the resulting imines with the Danishefsky diene **2** were defined as those shown in Table 2. Note that the use of triethylamine as an additive[14] is critical for the success of the reaction.

Table 1 Effects of Lewis acid and solvent



Entry	Lewis acid	Solvent	Yield[a]/%
1	BF_3-OEt_2	CH_2Cl_2	39
2	TMSOTf	CH_2Cl_2	35
3	$TiCl_4$	CH_2Cl_2	22
4	$ZnCl_2$	CH_2Cl_2	59
5	$ZnCl_2$	THF	74
6	$ZnCl_2$	CH_3CN	78
7	$ZnCl_2$	Et_2O	Trace
8	$ZnCl_2$	Toluene	No product
9	$ZnCl_2$	MeOH	80

[a] Isolated yield.

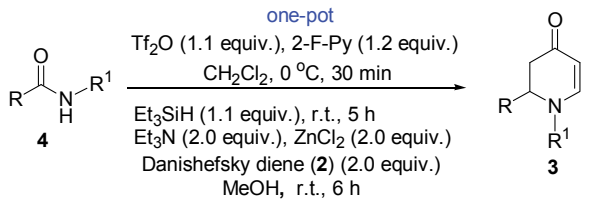
With the optimal conditions defined, a survey of the secandary amide for the reductive cycloaddition was carried out (Table 2). *N*-Alkyl substituents such as Me, phenethyl, and allyl groups were tolerated (Entries 2~4). In the latter case diene **2** reacted preferably with the amide over the terminal alkene. The use of a benzyl group or a secondary alkyl substituent (*i*-Pr) led to diminished yields (Entries 5 and 6) probably because of the increased steric hindrance. Note that amide **4g** reacted successfully in the presence of an ester functionality (Entry 7).

We next examined the effect of the aryl substituents on the reductive cycloaddition reaction (Entries 8~15). The reaction is compatible with the use of electron-donating substituents such as Me and OMe, and halogens such as F and Cl at various positions of the phenyl ring. The reason for the low yield of the 4-methoxylated substrate **4k** is unclear.

The reaction of *N*-*n*-butyl-2-naphthamide (**4p**) proceeded smoothly to yield **3p** in 76% yield (Entry 16). 2-Thiophenoylamide (**4q**) was less efficient and afforded **3q** in only 22% yield (Entry 17). Note that Frost reported that 2-thiophenecarboxaldehyde failed to undergo the three-component aza-Diels-Alder reaction with the Danishefsky diene.[23]

The chemoselectivity[24] is of great importance when it comes to the manipulation of structurally complex molecules. But it has rarely been demonstrated in the aza-Diels-Alder reactions. In addition to the chemoselective reaction showed in Entry 7, further investigation revealed that our one-pot reaction proceeded selectively in the presence of other potential dienophiles such as a cyano group, a ketone, and even an aldehyde (Entries 18~20).

Table 2 Scope of the one-pot reductive cycloaddition of *sec*-amides

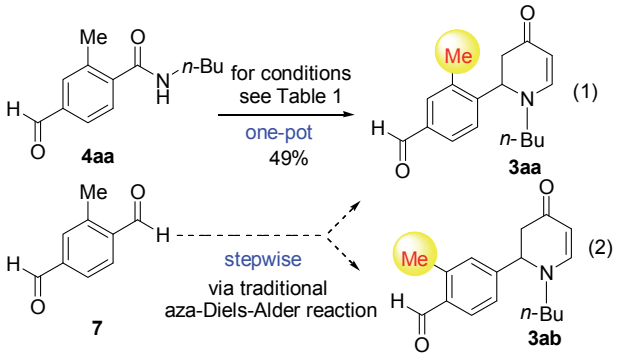


Entry	R	R^1	Product	Yield[a]/%
1	Ph	*n*-Bu	**3a**	80
2	Ph	Me	**3b**	77
3	Ph	$PhCH_2CH_2$	**3c**	65
4	Ph	Allyl	**3d**	73
5	Ph	Bn	**3e**	42
6	Ph	*i*-Pr	**3f**	31
7	Ph	$MeO_2CCH_2CH_2$	**3g**	68
8	4-MeC_6H_4	*n*-Bu	**3h**	83
9	3-MeC_6H_4	*n*-Bu	**3i**	81
10	2-MeC_6H_4	*n*-Bu	**3j**	67
11	4-$MeOC_6H_4$	*n*-Bu	**3k**	34
12	3,4,5-$(MeO)_3C_6H_2$	*n*-Bu	**3l**	70
13	4-FC_6H_4	*n*-Bu	**3m**	69
14	4-ClC_6H_4	*n*-Bu	**3n**	61
15	2-ClC_6H_4	*n*-Bu	**3o**	56
16	2-Naphth	*n*-Bu	**3p**	76
17	2-Thienyl	*n*-Bu	**3q**	22
18	4-NCC_6H_4	*n*-Bu	**3r**	43
19	4-$MeC(O)C_6H_4$	*n*-Bu	**3s**	60[b]
20	4-$HC(O)C_6H_4$	*n*-Bu	**3t**	58[b]
21	*n*-$C_{10}H_{21}$	*n*-Bu	**3u**	45
22	Me	*n*-Bu	**3v**	43
23	3,4-$(MeO)_2C_6H_3$	$Cl(CH_2)_4$	**3w**	53
24	3,4-$(MeO)_2C_6H_3$	$Br(CH_2)_4$	**3x**	50
25	3,4-$(MeO)_2C_6H_3$	$I(CH_2)_4$	**3y**	32
26	Me	$Cl(CH_2)_4$	**3z**	42

[a] Isolated yield. [b] Activation of amide was carried out at −78 ℃ for 1 h, then at 0 ℃ for 10 min, the reduction with Et_3SiH was performed at r.t. for 5 h.

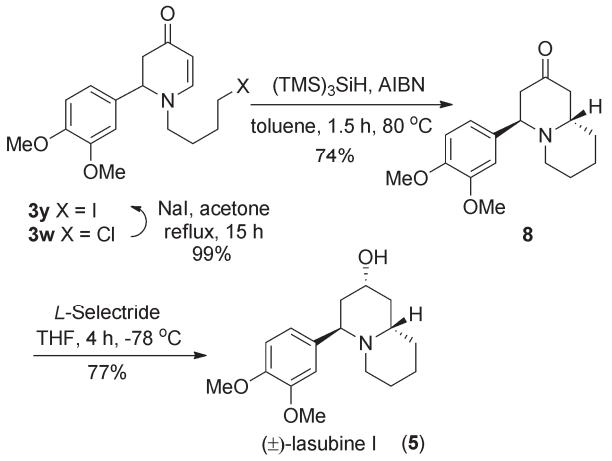
Aliphatic secondary amides **4u** and **4v** also reacted successfully to afford the corresponding dihydropyridinones **3u** and **3v** in moderate yields (Entries 21～22). It is noteworthy that the one-pot reductive cycloaddition tolerated amides bearing halo-substituted *N*-alkyl groups (**4w**～**4z**, Entries 23～26, cf. SI). Such chemoselectivity is important for further synthetic transformations.

The additional advantage of this one-pot reaction over the traditional aza-Diels-Alder reaction was demonstrated by the chemoselective reductive cycloaddition of **4aa**. Under the standard reaction conditions, **4aa** reacted to produce the desired **3aa** in 49% yield (Scheme 3, Eq. 1). Such selectivity would be difficult to achieve by the traditional stepwise aza-Diels-Alder reaction of **7** (Scheme 3, Eq. 2).



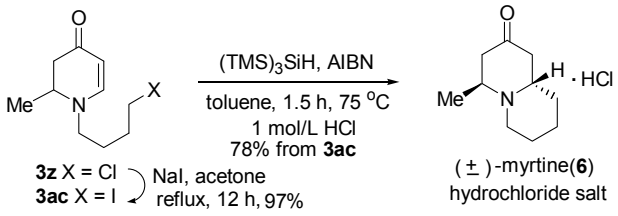
Scheme 3 Chemoselective approach to **3aa**

To demonstrate the synthetic potential of the chemoselective aza-Diels-Alder reactions, the transformation of adducts to alkaloids lasubine I (**5**) and myrtine (**6**) were envisioned. Lasubine I (**5**) and myrtine (**6**) are quinolizidine alkaloids isolated from the plant *Lagerstroemia subcostata*[25a] and *Vaccinium myrtillus*,[25b] respectively. Quinolizidine alkaloids are a class of natural products possessing numerous biological activities, such as antiinflammatory, antispasmodic, and diuretic properties.[26] The synthesis of quinolizidine alkaloids including lasubine I (**5**)[27] and myrtine[28] have attracted much attention. In the event, 2,3-dihydro-4-pyridone **3y**, which is also available from chloride **3w** (NaI in acetone, reflux, 15 h) in 99% yield, was treated with $(TMS)_3SiH$ (5 equiv.) and AIBN (3 equiv.) in toluene (1.5 h, 80 ℃)[29] to afford the known quinolizidinone **8**[27d] as the single diastereomer in 74% yield (Scheme 4). Reduction of **8** with *L*-Selectride[27d～27f,27h] afforded (±)-lasubine I (**5**) as a single diastereomer in 77% yield. The spectral data (^1H and ^{13}C NMR) of our synthetic product matches those reported.[27f]



Scheme 4 Transformation of 2,3-dihydro-4-pyridone **3y** to (±)-lasubine I (**5**)

Similarly, 2,3-dihydro-4-pyridone **3z** was converted to (±)-myrtine (**6**) by a two-step sequence (Scheme 5). Iodination (NaI, acetone, reflux, 12 h) of **3z** produced **3ac** in 97% yield. Free-radical cyclization of iodide **3ac** [$(TMS)_3SiH$ (5 equiv.), AIBN (3 equiv.), 1.5 h, 75 ℃] gave (±)-myrtine (**6**) as a single diastereomer in 78% yield.



Scheme 5 Transformation of 2,3-dihydro-4-pyridone **3z** to (±)-myrtine (**6**)

3 Conclusions

In summary, we have developed a one-pot procedure for the reductive cycloaddition of common secondary amides with the Danishefsky diene. The reaction is chemoselective for secondary amide without affecting sensitive carbonyl groups of aldehyde, ketone, ester and cyano group, and provides a rapid access to a variety of 1,2-disubstituted 2,3-dihydro-4-pyridones. The new procedure also affords the advantage of allow accessing to functionalized dihydropyridinones that are inaccessible selectively by the conventional aza-Diels-Alder reactions. The potential of the chemoselective aza-Diels-Alder reaction was demonstrated by the short protecting-group-free total syntheses of racemic lasubine I and myrtine.

3.1 Experimental section

General ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker spectrometer at a Bruker 400 (^{1}H/400 MHz, ^{13}C/100 MHz) or Bruker 600 (^{1}H/600 MHz, ^{13}C/150 MHz) spectrometer, respectively. Chemical shifts (δ) are reported in ppm and referenced to internal standard Me_4Si and solvent signals respectively (Me_4Si, δ 0 for ^{1}H NMR and $CDCl_3$, δ 77.0 for ^{13}C NMR). HRMS spectra were recorded on an ESI-TOF mass spectrometer. Melting points were determined on a Büchi M560 Automatic Melting Point apparatus. Infrared spectra were measured with a Nicolet Avatar 330 FT-IR spectrometer using film KBr pellet technique. Silica gel (300～400 mesh) was used for flash column chromatography (FC), eluting (unless otherwise stated) with ethyl acetate/hexane mixture. Trifluoromethanesulfonic anhydride (Tf_2O) was distilled over phosphorous pentoxide and used within a week. Dichloromethane was distilled over calcium hydride under N_2. Methanol was distilled over Mg under N_2.

3.1.1 General procedure for the one-pot synthesis of 2,3-dihydro-4-pyridones from secondary amides

Trifluoromethanesulfonic anhydride (Tf_2O) (46 μL, 0.27 mmol, 1.1 equiv.) was added dropwise to a cooled (0 ℃) solution of a secondary amide (0.25 mmol, 1.0 equiv.) and 2-fluoropyridine (26 μL, 0.30 mmol, 1.2 equiv.) in dichloromethane (2.0 mL). After being stirred for 30 min at 0 ℃, triethylsilane (44 μL, 0.28 mmol, 1.1 equiv.) was added at 0 ℃. The reaction mixture was warmed to room temperature and stirred for 5 h. The solvent was removed via a dry tube (anhydrous calcium chloride) under reduced pressure. To the residue were added successively CH_3OH (2.0 mL freshly distilled over Mg), Et_3N (70 μL, 0.50 mmol, 2.0 equiv.) and $ZnCl_2$ (0.50 mL, 1.00 mmol, 2.0 equiv., 1.0 mol/L in diethyl ether) at 0 ℃. The reaction mixture was stirred for 15 min and then to which Danishefsky's diene (97 μL, 0.50 mmol, 2.0 equiv.) was added. After being stirred for 6 h at r.t., the reaction was quenched with 1.0 mL of 1.0 mol/L HCl and extracted with dichloromethane (10 mL×3). The combined organic layers were washed successively with a saturated aqueous solution of $NaHCO_3$ (1.0 mL) and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel to afford the desired 2,3-dihydro-4-pyridone derivative.

3.1.2 1-Butyl-2-phenyl-2,3-dihydropyridin-4(1*H*)-one (**3a**)

Following the general procedure, the reductive cycloaddition of *N*-butylbenzamide (**4a**) (44 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc) ∶ *V*(*n*-hexane) = 1 ∶ 5], the known dihydropyridone **3a**[17m] (46 mg, yield 80%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.88 (t, J=7.3 Hz, 3H), 1.19～1.35 (m, 2H), 1.47～1.55 (m, 2H), 2.67 (dd, J=16.4, 7.8 Hz, 1H), 2.87 (dd, J=16.4, 7.0 Hz, 1H), 3.06～3.10 (m, 2H), 4.61 (dd, J=7.8, 7.0 Hz, 1H), 5.01 (d, J=7.5 Hz, 1H), 7.15 (d, J=7.5 Hz, 1H), 7.28～7.37 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.6, 19.7, 30.7, 43.7, 53.3, 60.9, 97.9, 126.8 (2C), 128.1, 128.9 (2C), 138.7, 154.0, 190.0; IR (film) ν_{max}: 3028, 2958, 2929, 2872, 1636, 1593, 1579, 1456, 1384, 1350, 1216, 1174, 1040, 940 cm^{-1}; HRMS (ESI) calcd for $[C_{15}H_{19}NONa]^+$ (M+Na$^+$) 252.1359; found 252.1365.

3.1.3 1-Methyl-2-phenyl-2,3-dihydropyridin-4(1*H*)-one (**3b**)

Following the general procedure, the reductive cycloaddition of *N*-methylbenzamide (**4b**) (34 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc) ∶ *V*(*n*-hexane) = 1 ∶ 2], the known dihydropyridone **3b**[18b] (36 mg, yield 77%) as a pale yellow solid, m.p. 107～109 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.69 (dd, J=16.4, 9.4 Hz, 1H), 2.82 (dd, J=16.4, 6.8 Hz, 1H), 2.83 (s, 3H), 4.48 (dd, J=9.4, 6.8 Hz, 1H), 5.02 (d, J=7.6 Hz, 1H), 7.10 (d, J=7.6 Hz, 1H), 7.28～7.40 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 41.3, 43.8, 63.6, 98.3, 126.9 (2C), 128.3, 129.0 (2C), 138.7, 155.1, 190.4; IR (film) ν_{max}: 3028, 2919, 2851, 1635, 1591, 1419, 1371, 1344, 1182, 1068, 978, 903 cm^{-1}; HRMS (ESI) calcd for $[C_{12}H_{13}NONa]^+$ (M+Na$^+$) 210.0889; found 210.0893.

3.1.4 1-Phenethyl-2-phenyl-2,3-dihydropyridin-4(1*H*)-one (**3c**)

Following the general procedure, the reductive cycloaddition of *N*-phenethylbenzamide (**4c**) (56 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc) ∶ *V*(*n*-hexane) = 1 ∶ 5], the desired dihydropyridone **3c** (45 mg, yield 65%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.65 (dd, J=16.4, 8.3 Hz, 1H), 2.73～2.85 (m, 3H), 3.27～3.37 (m, 2H), 4.53 (dd, J=8.3, 6.9 Hz, 1H), 4.97 (d, J=7.6 Hz, 1H), 7.02 (d, J=7.6 Hz, 1H), 7.04～7.08 (m, 2H), 7.24～7.39 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 30.6, 43.7, 55.0, 61.5, 98.5, 126.8 (2C), 127.0 (2C), 128.3 (2C), 128.7 (2C), 129.0 (2C), 137.8, 138.6, 153.8, 190.2; IR (film) ν_{max}: 3025,

2921, 2852, 1637, 1578, 1453, 1360, 1162, 1043, 902, 834 cm^{-1}; HRMS (ESI) calcd for $[C_{19}H_{19}NONa]^+$ ($M+Na^+$) 300.1359; found 300.1362.

3.1.5 1-Allyl-2-phenyl-2,3-dihydropyridin-4(1*H*)-one (**3d**)

Following the general procedure, the reductive cycloaddition of *N*-allylbenzamide (**4d**) (40 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc) ∶ *V*(*n*-hexane) = 1 ∶ 5], the known dihydropyridone **3d**[17c] (39 mg, yield 73%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.70 (dd, J=16.5, 8.4 Hz 1H), 2.86 (dd, J=16.5, 7.0 Hz, 1H), 3.53～3.61 (m, 1H), 3.68～3.78 (m, 1H), 4.61 (dd, J=8.4, 7.0 Hz, 1H), 5.07 (d, J=7.7 Hz, 1H), 5.12～5.19 (m, 1H), 5.22～5.27 (m, 1H), 5.70～5.81 (m, 1H), 7.17 (d, J=7.7 Hz, 1H), 7.27～7.39 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 43.7, 55.5, 61.1, 98.9, 119.0, 126.9 (2C), 128.2, 129.0 (2C), 132.6, 138.7, 153.8, 190.3; IR (film) ν_{max}: 3058, 3030, 2918, 2851, 1639, 1590, 1452, 1381, 1354, 1219, 1163, 1040, 993, 931 cm^{-1}; HRMS (ESI) calcd for $[C_{14}H_{15}NONa]^+$ ($M+Na^+$) 236.1046; found 236.1047.

3.1.6 1-Benzyl-2-phenyl-2,3-dihydropyridin-4(1*H*)-one (**3e**)

Following the general procedure, the reductive cycloaddition of *N*-benzylbenzamide (**4e**) (53 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc) ∶ *V*(*n*-hexane) = 1 ∶ 5], the known dihydropyridone **3e**[17c] (28 mg, yield 42%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.69 (dd, J=16.5, 8.1 Hz, lH), 2.81 (dd, J=16.5, 7.1 Hz, 1H), 4.12 (d, J=15.1 Hz, 1H), 4.34 (d, J=15.1 Hz, 1H), 4.50 (dd, J=8.1, 7.1 Hz, 1H), 5.09 (d, J=7.7 Hz, 1H), 7.11～7.15 (m, 2H), 7.23～7.39 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 43.7, 57.2, 60.8, 98.8, 127.1 (2C), 127.7 (2C), 128.2, 128.3, 128.9 (2C), 129.0 (2C), 135.9, 138.6, 154.1, 190.3; IR (film) ν_{max}: 3029, 2922, 2852, 1640, 1589, 1494, 1450, 1381, 1356, 1208, 1157, 1040, 951 cm^{-1}; HRMS (ESI) calcd for $[C_{18}H_{17}NONa]^+$($M+Na^+$) 286.1202; found 286.1205.

3.1.7 1-Isopropyl-2-phenyl-2,3-dihydropyridin-4(1*H*)-one (**3f**)

Following the general procedure, the reductive cycloaddition of *N*-isopropylbenzamide (**4f**) (41 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc) ∶ *V*(*n*-hexane) = 1 ∶ 2], the known dihydropyridone **3f**[17c] (17 mg, yield 31%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.13 (d, J=6.5 Hz, 3H), 1.24 (d, J=6.8 Hz, 3H), 2.65 (dd, J=16.4, 7.8 Hz, 1H), 2.87 (dd, J=16.4, 6.9 Hz, 1H), 3.32～3.42 (m, 1H), 4.64 (dd, J=7.8, 6.9 Hz, 1H), 5.09 (d, J=7.6 Hz, 1H), 7.27 (d, J=7.6 Hz, 1H), 7.29～7.37 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.5, 21.6, 44.1, 52.5, 61.1, 98.7, 126.6 (2C), 128.1, 129.0 (2C), 139.7, 149.9, 190.1; IR (film) ν_{max}: 3029, 2971, 2926, 1638, 1578, 1494, 1452, 1404, 1300, 1253, 1226, 1184, 1158, 1061, 978, 925 cm^{-1}; HRMS (ESI) calcd for $[C_{14}H_{17}NONa]^+$ ($M+Na^+$) 238.1202; found 238.1203.

3.1.8 Methyl 3-(4-oxo-2-phenyl-3,4-dihydropyridin-1(2*H*)-yl) propanoate (**3g**)

Following the general procedure, the reductive cycloaddition of methyl 3-benzamidopropanoate (**4g**) (52 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc) ∶ *V*(*n*-hexane) = 1 ∶ 2], the desired dihydropyridone **3g** (44 mg, yield 68%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.40～2.58 (m, 2H), 2.66 (dd, J=16.4, 7.7 Hz, 1H), 2.86 (dd, J=16.4, 6.9 Hz, 1H), 3.31～3.41 (m, 1H), 3.47～3.56 (m, 1H), 3.67 (s, 3H), 4.64 (dd, J=7.7, 6.9 Hz, 1H), 5.03 (d, J=7.7 Hz, 1H), 7.21 (d, J=7.7 Hz, 1H), 7.28～7.39 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 33.2, 43.7, 49.0, 51.9, 60.8, 98.9, 126.7 (2C), 128.3, 129.0 (2C), 138.4, 153.9, 171.2, 190.0; IR (film) ν_{max}: 3026, 2950, 2921, 2850, 1735, 1639, 1592, 1494, 1442, 1384, 1257, 1199, 1164, 1053, 982, 839 cm^{-1}; HRMS (ESI) calcd for $[C_{15}H_{17}NO_3Na]^+$ ($M+Na^+$) 282.1101; found 282.1104.

3.1.9 1-Butyl-2-(*p*-tolyl)-2,3-dihydropyridin-4(1*H*)-one (**3h**)

Following the general procedure, the reductive cycloaddition of *N*-butyl-4-methylbenzamide (**4h**) (48 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc) ∶ *V*(*n*-hexane) = 1 ∶ 5], the desired dihydropyridone **3h** (50 mg, yield 83%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.88 (t, J=7.3 Hz, 3H), 1.18～1.34 (m, 2H), 1.45～1.54 (m, 2H), 2.33 (s, 3H), 2.66 (dd, J=16.4, 8.2 Hz 1H), 2.84 (dd, J=16.4, 7.0 Hz, 1H), 3.04～3.10 (m, 2H), 4.58 (dd, J=8.2, 7.0 Hz, 1H), 5.00 (d, J=7.5 Hz, 1H), 7.13～7.22 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.6, 19.7, 21.0, 30.7, 43.8, 53.2, 60.7, 97.8, 126.8 (2C), 129.5 (2C), 135.7, 137.9, 154.0, 190.2; IR (film) ν_{max}: 3020, 2958, 2928, 2868, 1641, 1592, 1512, 1382, 1347, 1257, 1214, 1171, 1113, 1082, 985, 817 cm^{-1}; HRMS (ESI) calcd for $[C_{16}H_{21}NONa]^+$ ($M+Na^+$) 266.1515; found 266.1521.

3.1.10 1-Butyl-2-(*m*-tolyl)-2,3-dihydropyridin-4(1*H*)-one (**3i**)

Following the general procedure, the reductive cycloaddition of *N*-butyl-3-methylbenzamide (**4i**) (48 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc) ∶ *V*(*n*-hexane) = 1 ∶ 5], the desired dihydropyridone **3i** (49 mg, yield 81%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.88 (t, J=7.3 Hz, 3H), 1.18～1.38 (m, 2H), 1.46～1.55 (m, 2H), 2.35 (s, 3H), 2.66 (dd, J=16.4, 8.0 Hz, 1H), 2.86 (dd, J=16.4, 7.0 Hz, 1H), 3.05～3.11 (m, 2H), 4.57 (dd, J=8.0, 7.0 Hz, 1H), 5.01 (d, J=7.6 Hz, 1H), 7.06～7.13 (m, 3H), 7.15 (d, J=7.6 Hz, 1H), 7.20～7.26 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.5, 19.6, 21.4, 30.7, 43.6, 53.2, 60.8, 97.8, 123.8, 127.4, 128.7, 128.8, 138.6 (2 C), 154.0, 190.0; IR (film) ν_{max}: 3026, 2958, 2927, 2867, 1640, 1588, 1457, 1382, 1346, 1290, 1217, 1173, 1080, 934, 877 cm^{-1}; HRMS (ESI) calcd for $[C_{16}H_{21}NONa]^+$ ($M+Na^+$) 266.1515; found 266.1521.

3.1.11 1-Butyl-2-(*o*-tolyl)-2,3-dihydropyridin-4(1*H*)-one (**3j**)

Following the general procedure, the reductive cycloaddition of *N*-butyl-2-methylbenzamide (**4j**) (48 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc) ∶ *V*(*n*-hexane) = 1 ∶ 5], the desired dihydropyridone **3j** (41 mg, yield 67%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.87 (t, J=7.3 Hz, 3H), 1.16～1.35 (m, 2H), 1.41～1.52 (m, 2H), 2.34 (s, 3H),

2.61 (dd, J=16.5, 9.0 Hz, 1H), 2.79 (dd, J=16.5, 7.2 Hz, 1H), 3.02～3.08 (m, 2H), 4.86 (dd, J=9.0, 7.2 Hz, 1H), 5.02 (d, J=7.5 Hz, 1H), 7.16～7.24 (m, 4H), 7.31～7.35 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.6, 19.0, 19.7, 30.5, 42.3, 53.1, 57.3, 97.7, 126.4, 126.5, 127.8, 131.2, 134.8, 136.4, 154.7, 190.0; IR (film) ν_{max}: 3064, 3018, 2957, 2925, 2862, 1640, 1588, 1456, 1382, 1291, 1254, 1216, 1172, 1044, 902 cm^{-1}; HRMS (ESI) calcd for $[C_{16}H_{21}NONa]^+$ (M+Na$^+$) 266.1515; found 266.1515.

3.1.12 1-Butyl-2-(*p*-methoxyphenyl)-2,3-dihydropyridin-4(1*H*)-one (**3k**)

Following the general procedure, the reductive cycloaddition of *N*-butyl-4-methoxybenzamide (**4k**) (52 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc)∶*V*(*n*-hexane)=1∶5], the desired dihydropyridone **3k** (22 mg, yield 34%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.88 (t, J=7.3 Hz, 3H), 1.16～1.36 (m, 2H), 1.44～1.54 (m, 2H), 2.66 (dd, J=16.4, 8.4 Hz, 1H), 2.82 (dd, J=16.4, 6.8 Hz, 1H), 3.03～3.09 (m, 2H), 3.80 (s, 3H), 4.56 (dd, J=8.4, 6.8 Hz, 1H), 5.00 (d, J=7.5 Hz, 1H), 6.85～6.91 (m, 2H), 7.14 (d, J=7.5 Hz, 1H), 7.20～7.25 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.6, 19.7, 30.8, 43.9, 53.1, 55.3, 60.5, 97.9, 114.3 (2C), 128.1 (2C), 130.8, 154.0, 159.5, 190.4; IR (film) ν_{max}: 3006, 2958, 2922, 2853, 1640, 1588, 1511, 1459, 1381, 1295, 1251, 1214, 1173, 1111, 1032, 902, 832 cm^{-1}; HRMS (ESI) calcd for $[C_{16}H_{21}NO_2Na]^+$ (M+Na$^+$) 282.1465; found 282.1467.

3.1.13 1-Butyl-2-(3,4,5-trimethoxyphenyl)-2,3-dihydropyridin-4(1*H*)-one (**3l**)

Following the general procedure, the reductive cycloaddition of *N*-butyl-3,4,5-trimethoxybenzamide (**4l**) (67 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc)∶*V*(*n*-hexane)=1∶2], the desired dihydropyridone **3l** (56 mg, yield 70%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.89 (t, J=7.3 Hz, 3H), 1.20-1.34 (m, 2H), 1.49～1.54 (m, 2H), 2.66 (dd, J=16.5, 8.0 Hz, 1H), 2.86 (dd, J=16.5, 7.2 Hz, 1H), 3.08～3.13 (m, 2H), 3.84 (s, 9H), 4.54 (dd, J=8.0, 7.2 Hz, 1H), 4.99 (d, J=7.3 Hz, 1H), 6.51 (s, 2H), 7.18 (d, J=7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.5, 19.7, 30.8, 43.5, 53.3, 56.1(2C), 60.7, 61.1, 97.7, 103.9 (2C), 134.4, 137.8, 153.5 (2C), 154.4, 190.3; IR (film) ν_{max}: 3073, 2956, 2933, 2866, 2834, 1638, 1590, 1506, 1459, 1423, 1327, 1240, 1173, 1126, 1007, 835 cm^{-1}; HRMS (ESI) calcd for $[C_{18}H_{25}NO_4Na]^+$ (M+Na$^+$) 342.1676; found 342.1674.

3.1.14 1-Butyl-2-(*p*-fluorophenyl)-2,3-dihydropyridin-4(1*H*)-one (**3m**)

Following the general procedure, the reductive cycloaddition of *N*-butyl-4-fluorobenzamide (**4m**) (49 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc)∶*V*(*n*-hexane)=1∶5], the desired dihydropyridone **3m** (43 mg, yield 69%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.89 (t, J=7.3 Hz, 3H), 1.18～1.38 (m, 2H), 1.46～1.56 (m, 2H), 2.62 (dd, J=16.4, 7.4 Hz, 1H), 2.88 (dd, J=16.4, 7.0 Hz, 1H), 3.01～3.15 (m, 2H), 4.61 (dd, J=7.4, 7.0 Hz, 1H), 5.01 (d, J=7.6 Hz, 1H), 7.01～7.07 (m, 2H), 7.16 (d, J=7.6 Hz, 1H), 7.25～7.31 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.6, 19.7, 30.8, 43.6, 53.3, 60.2, 98.0, 115.9 (d, $J_{F\text{-}C}$=21.7 Hz, 2C), 128.4 (d, $J_{F\text{-}C}$=8.1 Hz, 2C), 134.6 (d, $J_{F\text{-}C}$=3.3 Hz), 153.9, 162.4 (d, $J_{F\text{-}C}$=249.0 Hz), 189.8; IR (film) ν_{max}: 3037, 2959, 2923, 2854, 1640, 1585, 1508, 1459, 1381, 1295, 1221, 1166, 1041, 836 cm^{-1}; HRMS (ESI) calcd for $[C_{15}H_{18}FNONa]^+$ (M+Na$^+$) 270.1265; found 270.1267.

3.1.15 1-Butyl-2-(*p*-chlorophenyl)-2,3-dihydropyridin-4(1*H*)-one (**3n**)

Following the general procedure, the reductive cycloaddition of *N*-butyl-4-chlorobenzamide (**4n**) (53 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc)∶*V*(*n*-hexane)=1∶5], the desired dihydropyridone **3n** (40 mg, yield 61%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.89 (t, J=7.3 Hz, 3H), 1.20～1.38 (m, 2H), 1.46～1.56 (m, 2H), 2.60 (dd, J=16.4, 7.1 Hz, 1H), 2.89 (dd, J=16.4, 7.2 Hz, 1H), 3.00～3.16 (m, 2H), 4.59 (dd, J=7.2, 7.1 Hz, 1H), 5.01 (d, J=7.6 Hz, 1H), 7.16 (d, J=7.6 Hz, 1H), 7.22～7.36 (m, 2H), 7.30～7.35 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.6, 19.6, 30.7, 43.4, 53.4, 60.1, 98.1, 128.1 (2C), 129.1 (2C), 133.9, 137.3, 153.8, 189.5; IR (film) ν_{max}: 3031, 2958, 2925, 2866, 1639, 1589, 1489, 1458, 1382, 1214, 1170, 1088, 1014, 982, 825 cm^{-1}; HRMS (ESI) calcd for $[C_{15}H_{18}ClNONa]^+$ (M+Na$^+$) 286.0969; found 286.0968.

3.1.16 1-Butyl-2-(*o*-chlorophenyl)-2,3-dihydropyridin-4(1*H*)-one (**3o**)

Following the general procedure, the reductive cycloaddition of *N*-butyl-2-chlorobenzamide (**4o**) (53 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc)∶*V*(*n*-hexane)=1∶5], the desired dihydropyridone **3o** (37 mg, yield 56%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.91 (t, J=7.3 Hz, 3H), 1.22～1.42 (m, 2H), 1.50～1.58 (m, 2H), 2.65 (dd, J=16.5, 5.6 Hz, 1H), 2.97 (dd, J=16.5, 7.9 Hz, 1H), 3.01～3.18 (m, 2H), 5.00 (d, J=7.6 Hz, 1H), 5.12 (dd, J=7.9, 5.6 Hz, 1H), 7.20～7.26 (m, 3H), 7.37～7.41 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.6, 19.7, 30.8, 41.2, 53.8, 56.9, 97.7, 127.2, 127.7, 129.2, 130.3, 132.6, 135.6, 154.1, 189.4; IR (film) ν_{max}: 3064, 2958, 2923, 2855, 1641, 1591, 1463, 1383, 1347, 1214, 1171, 1041 cm^{-1}; HRMS (ESI) calcd for $[C_{15}H_{18}ClNONa]^+$ (M+Na$^+$) 286.0969; found 286.0971.

3.1.17 1-Butyl-2-(naphthalen-2-yl)-2,3-dihydropyridin-4(1*H*)-one (**3p**)

Following the general procedure, the reductive cycloaddition of *N*-butyl-2-naphthamide (**4p**) (57 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc)∶*V*(*n*-hexane)=1∶5], the desired dihydropyridone **3p** (53 mg, yield 76%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.85 (t, J=7.3 Hz, 3H), 1.16～1.36 (m, 2H), 1.44～1.62 (m, 2H), 2.88～2.99 (m, 2H), 3.01～3.20 (m, 2H), 5.06 (d, J=7.6 Hz, 1H), 5.40 (dd, J=7.7, 7.6 Hz, 1H), 7.30 (d, J=7.6 Hz, 1H), 7.40～7.48 (m, 2H), 7.49～7.58 (m, 2H), 7.79～7.85 (m, 1H), 7.88～7.93 (m, 1H), 8.00～8.07 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.6, 19.8, 31.0, 42.4, 53.6, 58.3, 97.7, 122.5, 124.7, 125.3, 125.8, 126.5, 128.9, 129.4, 130.3, 132.8, 134.4, 154.4, 190.0; IR (film) ν_{max}: 3049, 2958, 2927, 2668, 1640, 1588, 1511, 1461, 1371, 1323, 1261,

1217, 1178, 1042, 965, 931, 905, 859, 799 cm^{-1}; HRMS (ESI) calcd for $[C_{19}H_{21}NONa]^+$ (M+Na^+) 302.1515; found 302.1520.

3.1.18 1-Butyl-2-(thiophen-2-yl)-2,3-dihydropyridin-4(1*H*)-one (**3q**)

Following the general procedure, the reductive cycloaddition of *N*-butylthiophene-2-carboxamide (**4q**) (46 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc)∶*V*(*n*-hexane)=1∶5], the desired dihydropyridone **3q** (13 mg, yield 22%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 0.93 (t, *J*=7.3 Hz, 3H), 1.26～1.42 (m, 2H), 1.53～1.66 (m, 2H), 2.71 (dd, *J*=16.3, 5.8 Hz, 1H), 2.97 (dd, *J*=16.3, 6.8 Hz, 1H), 3.07～3.26 (m, 2H), 4.87 (dd, *J*=6.8, 5.8 Hz, 1H), 5.05 (d, *J*=7.5 Hz, 1H), 6.92～6.97 (m, 1H), 6.99～7.05 (m, 2H), 7.22～7.26 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 13.6, 19.7, 31.1, 43.7, 53.4, 56.4, 98.4, 125.4, 126.1, 126.5, 141.5, 152.8, 189.7; IR (film) ν_{max}: 3074, 2953, 2926, 2856, 1720, 1641, 1588, 1460, 1377, 1313, 1213, 1170, 1077, 1043, 970, 849 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_{17}NOSNa]^+$ (M+Na^+) 258.0923; found 258.0928.

3.1.19 1-Butyl-2-(*p*-cyanophenyl)-2,3-dihydropyridin-4(1*H*)-one (**3r**)

Following the general procedure, the reductive cycloaddition of *N*-butyl-4-cyanobenzamide (**4r**) (51 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc)∶*V*(*n*-hexane)=1∶2], the desired dihydropyridone **3r** (27 mg, yield 43%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 0.91 (t, *J*=7.3 Hz, 3H), 1.23～1.41 (m, 2H), 1.49～1.60 (m, 2H), 2.58 (dd, *J*=16.4, 5.8 Hz, 1H), 2.95～3.10 (m, 2H), 3.13～3.23 (m, 1H), 4.68 (dd, *J*=7.1, 5.8 Hz, 1H), 5.03 (d, *J*=7.6 Hz, 1H), 7.20 (d, *J*=7.6 Hz, 1H), 7.39～7.45 (m, 2H), 7.63～7.70 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 13.6, 19.7, 30.9, 42.9, 53.9, 60.2, 98.5, 112.1, 118.2, 127.4 (2C), 132.8 (2C), 144.1, 153.6, 188.8; IR (film) ν_{max}: 3034, 2959, 2926, 2868, 2228, 1639, 1588, 1460, 1383, 1264, 1215, 1171, 1040, 982, 934, 836 cm^{-1}; HRMS (ESI) calcd for $[C_{16}H_{18}N_2ONa]^+$ (M+Na^+) 277.1311; found 277.1312.

3.1.20 2-(*p*-Acetylphenyl)-1-butyl-2,3-dihydropyridin-4(1*H*)-one (**3s**)

Following the general procedure, the activating temperature was changed to −78 ℃, the reductive cycloaddition of *N*-butyl-4-acetylbenzamide (**4s**) (55 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc)∶*V*(*n*-hexane)=1∶5], the desired dihydropyridone **3s** (41 mg, yield 60%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 0.90 (t, *J*=7.3 Hz, 3H), 1.20～1.41 (m, 2H), 1.48～1.58 (m, 2H), 2.63 (dd, *J*=16.4, 6.9 Hz, 1H), 2.60 (s, 3H), 2.93 (dd, *J*=16.4, 7.2 Hz, 1H), 3.02～3.20 (m, 2H), 4.68 (dd, *J*=7.2, 6.9 Hz, 1H), 5.03 (d, *J*=7.5 Hz, 1H), 7.18 (d, *J*=7.6 Hz, 1H), 7.36～7.44 (m, 2H), 7.92～7.98 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 13.5, 19.6, 26.5, 30.8, 43.2, 53.6, 60.4, 98.3, 126.9 (2C), 129.0 (2C), 136.9, 143.9, 153.7, 189.2, 197.3; IR (film) ν_{max}: 3037, 2959, 2927, 2866, 1683, 1639, 1589, 1459, 1411, 1358, 1266, 1214, 1171, 1079, 960, 833 cm^{-1}; HRMS (ESI) calcd for $[C_{17}H_{21}NO_2Na]^+$ (M+Na^+) 294.1465; found 294.1465.

3.1.21 1-Butyl-2-(*p*-formylphenyl)-2,3-dihydropyridin-4(1*H*)-one (**3t**)

Following the general procedure, the activating temperature was changed to −78 ℃, the reductive cycloaddition of *N*-butyl-4-formylbenzamide (**4t**) (51 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc)∶*V*(*n*-hexane)=1∶5], the desired dihydropyridone **3t** (37 mg, yield 58%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 0.90 (t, *J*=7.3 Hz, 3H), 1.22～1.40 (m, 2H), 1.49～1.59 (m, 2H), 2.64 (dd, *J*=16.4, 6.4 Hz, 1H), 2.97 (dd, *J*=16.4, 7.3 Hz, 1H), 3.02～3.22 (m, 2H), 4.70 (dd, *J*=7.3, 6.4 Hz, 1H), 5.04 (d, *J*=7.6 Hz, 1H), 7.19 (d, *J*=7.6 Hz, 1H), 7.45～7.50 (m, 2H), 7.86～7.91 (m, 2H), 10.01 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 13.6, 19.7, 30.9, 43.2, 53.8, 60.6, 98.5, 127.4 (2C), 130.4 (2C), 136.3, 145.6, 153.7, 189.1, 191.1; IR (film) ν_{max}: 3043, 2962, 2924, 2854, 1701, 1637, 1589, 1458, 1383, 1298, 1210, 1170, 1045, 833 cm^{-1}; HRMS (ESI) calcd for $[C_{16}H_{19}NO_2Na]^+$ (M+Na^+) 280.1308; found 280.1307.

3.1.22 1-Butyl-2-decyl-2,3-dihydropyridin-4(1*H*)-one (**3u**)

Following the general procedure, the reductive cycloaddition of *N*-butylundecanamide (**4u**) (60 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc)∶*V*(*n*-hexane)=1∶5], the desired dihydropyridone **3u** (33 mg, yield 45%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 0.88 (t, *J*=6.8 Hz, 3H), 0.97 (t, *J*=7.3 Hz, 3H), 1.19～1.45 (m, 17H), 1.54～1.64 (m, 4H), 1.69～1.80 (m, 1H), 2.34 (dd, *J*=16.3, 2.8 Hz, 1H), 2.72 (dd, *J*=16.3, 6.8 Hz, 1H), 3.12～3.26 (m, 2H), 3.38～3.48 (m, 1H), 4.87 (d, *J*=7.3 Hz, 1H), 6.92 (dd, *J*=7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 13.6, 14.0, 19.7, 22.6, 25.6, 28.5, 29.2, 29.4, 29.5 (3C), 31.8 (2C), 39.3, 53.8, 56.5, 96.3, 152.3, 190.4; IR (film) ν_{max}: 3028, 2956, 2926, 2855, 1642, 1588, 1459, 1382, 1215, 1175 cm^{-1}; HRMS (ESI) calcd for $[C_{19}H_{35}NONa]^+$ (M+Na^+) 316.2611; found 316.2618.

3.1.23 1-Butyl-2-methyl-2,3-dihydropyridin-4(1*H*)-one (**3v**)

Following the general procedure, the reductive cycloaddition of *N*-butylacetamide (**4v**) (29 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc)∶*V*(*n*-hexane)=1∶2], the desired dihydropyridone **3v** (18 mg, yield 43%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 0.96 (t, *J*=7.3 Hz, 3H), 1.24 (d, *J*=6.7 Hz, 3H), 1.33～1.43 (m, 2H), 1.55～1.63 (m, 2H), 2.22 (dd, *J*=16.3, 4.4 Hz, 1H), 2.73 (dd, *J*=16.3, 6.6 Hz, 1H), 3.09～3.18 (m, 1H), 3.19～3.27 (m, 1H), 3.60～3.69 (m, 1H), 4.90 (d, *J*=7.5 Hz, 1H), 6.90 (d, *J*=7.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 13.6, 15.2, 19.7, 31.4, 42.2, 52.0, 53.1, 96.5, 152.3, 190.5; IR (film) ν_{max}: 3031, 2961, 2928, 2870, 1640, 1586, 1456, 1380, 1345, 1272, 1220, 1177, 1118, 1029 cm^{-1}; HRMS (ESI) calcd for $[C_{10}H_{17}NONa]^+$ (M+Na^+) 190.1202; found 190.1201.

3.1.24 1-(4-Chlorobutyl)-2-(3,4-dimethoxyphenyl)-2,3-dihydropyridin-4(1*H*)-one (**3w**)

Following the general procedure, the reductive cycloaddition of *N*-(4-chlorobutyl)-3,4-dimethoxybenzamide (**4w**)

(544 mg, 2.00 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc)∶*V*(*n*-hexane)=1∶2], the known dihydropyridone **3w**[27i] (342 mg, yield 53%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.62～1.80 (m, 4H), 2.70 (dd, *J*=16.5, 9.0 Hz 1H), 2.82 (dd, *J*=16.5, 6.8 Hz, 1H), 3.04～3.18 (m, 2H), 3.45～3.55 (m, 2H), 3.87 (s, 3H), 3.88 (s, 3H), 4.56 (dd, *J*=9.0, 6.8 Hz, 1H), 5.04 (d, *J*=7.6 Hz, 1H), 6.81～6.88 (m, 3H), 7.15 (d, *J*=7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 25.6, 29.3, 43.9, 44.2, 52.5, 55.8, 55.9, 60.9, 98.3, 109.8, 111.3, 119.4, 131.4, 149.0, 149.3, 153.8, 190.3; IR (film) ν_{max}: 3072, 2919, 2849, 1638, 1584, 1515, 1459, 1385, 1261, 1175, 1141, 1025, 871 cm^{-1}; HRMS (ESI) calcd for $[C_{17}H_{22}ClNO_3Na]^+$ (M+Na$^+$) 346.1180; found 346.1180.

3.1.25 1-(4-Bromobutyl)-2-(3,4-dimethoxyphenyl)-2,3-dihydropyridin-4(1*H*)-one (**3x**)

Following the general procedure, the reductive cycloaddition of *N*-(4-bromobutyl)-3,4-dimethoxy- benzamide (**4x**) (315 mg, 1.00 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc)∶*V*(*n*-hexane)=1∶2], the desired dihydropyridone **3x** (184 mg, yield 50%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.64～1.74 (m, 2H), 1.75～1.87 (m, 2H), 2.70 (dd, *J*=16.4, 9.2 Hz, 1H), 2.81 (dd, *J*=16.4, 6.7 Hz, 1H), 3.03～3.18 (m, 2H), 3.30～3.42 (m, 2H), 3.87 (s, 3H), 3.88 (s, 3H), 4.55 (dd, *J*=9.2, 6.7 Hz, 1H), 5.05 (d, *J*=7.7 Hz, 1H), 6.81～6.89 (m, 3H), 7.13 (d, *J*=7.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 27.2, 29.5, 32.7, 44.0, 52.4, 55.9, 56.0, 61.1, 98.6, 110.0, 111.4, 120.0, 131.1, 149.1, 149.5, 153.8, 190.5; IR (film) ν_{max}: 3069, 2925, 2853, 1636, 1584, 1514, 1457, 1260, 1174, 1140, 1034 cm^{-1}; HRMS (ESI) calcd for $[C_{17}H_{22}BrNO_3Na]^+$ (M+Na$^+$) 390.0675; found 390.0679.

3.1.26 2-(3,4-Dimethoxyphenyl)-1-(4-iodobutyl)-2,3-dihydropyridin-4(1*H*)-one (**3y**)

Following the general procedure, the reductive cycloaddition of *N*-(4-iodobutyl)-3,4-dimethoxybenzamide (**4y**) (363 mg, 1.00 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc)∶*V*(*n*-hexane)=1∶2], the known dihydropyridone **3y**[27i] (133 mg, yield 32%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.60～1.88 (m, 4H), 2.70 (dd, *J*=16.4, 9.2 Hz, 1H), 2.81 (dd, *J*=16.4, 6.7 Hz, 1H), 3.01～3.20 (m, 4H), 3.88 (s, 3H), 3.89 (s, 3H), 4.56 (dd, *J*=9.2, 6.7 Hz, 1H), 5.04 (d, *J*=7.6 Hz, 1H), 6.82～6.90 (m, 3H), 7.13 (d, *J*=7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 5.5, 29.4, 30.1, 44.0, 52.1, 55.9, 56.0, 61.0, 98.5, 109.9, 111.4, 119.5, 131.1, 149.1, 149.5, 153.9, 190.3; IR (film) ν_{max}: 3009, 2921, 2852, 1631, 1571, 1514, 1462, 1260, 1139, 1089, 1023 cm^{-1}; HRMS (ESI) calcd for $[C_{17}H_{22}INO_3Na]^+$ (M+Na$^+$) 438.0537; found 438.0529.

3.1.27 1-(4-Chlorobutyl)-2-methyl-2,3-dihydropyridin-4(1*H*)-one (**3z**)

Following the general procedure, the reductive cycloaddition of *N*-(4-chlorobutyl)acetamide (**4z**) (240 mg, 1.60 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc)∶*V*(*n*-hexane)=1∶2], the desired dihydropyridone **3z** (135 mg, yield 42%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.25 (d, *J*=6.7 Hz, 3H), 1.73～1.90 (m, 4H), 2.23 (dd, *J*=16.3, 4.0 Hz 1H), 2.74 (dd, *J*=16.3, 6.6 Hz, 1H), 3.13～3.24 (m, 1H), 3.25～3.35 (m, 1H), 3.56～3.62 (m, 2H), 3.63～3.71 (m, 1H), 4.91 (d, *J*=7.4 Hz, 1H), 6.91 (d, *J*=7.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 15.1, 26.6, 29.3, 42.4, 44.2, 51.9, 52.6, 96.9, 152.1, 190.5; IR (film) ν_{max}: 3081, 2921, 2852, 1637, 1585, 1453, 1382, 1236 cm^{-1}; HRMS (ESI) calcd for $[C_{10}H_{16}ClNONa]^+$ (M+Na$^+$) 224.0813; found 224.0820.

3.1.28 1-Butyl-2-(4-formyl-2-methylphenyl)-2,3-dihydropyridin-4(1*H*)-one (**3aa**)

Following the general procedure, the activating temperature was changed to －78 ℃, the reductive cycloaddition of *N*-butyl-4-formyl-2-methylbenzamide (**4aa**) (55 mg, 0.25 mmol) gave, after flash column chromatography on silica gel [*V*(EtOAc)∶*V*(*n*-hexane)=1∶2], the desired dihydropyridone **3aa** (33 mg, yield 49%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.89 (t, *J*=7.3 Hz, 3H), 1.20～1.38 (m, 2H), 1.44～1.54 (m, 2H), 2.43 (s, 3H), 2.55 (dd, *J*=16.4, 7.8 Hz, 1H), 2.87 (dd, *J*=16.4, 7.5 Hz, 1H), 2.97～3.06 (m, 1H), 3.07～3.16 (m, 1H), 4.90 (dd, *J*=7.8, 7.5 Hz, 1H), 5.05 (d, *J*=7.6 Hz, 1H), 7.24 (d, *J*=7.6 Hz, 1H), 7.52～7.55 (m, 1H), 7.68～7.75 (m, 2H), 9.98 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.6, 19.1, 19.7, 30.6, 41.7, 53.6, 57.3, 98.2, 127.1, 128.0, 132.4, 136.0 (2C), 143.4, 154.5, 189.2, 191.7; IR (film) ν_{max}: 3046, 2958, 2927, 2869, 1692, 1638, 1590, 1457, 1385, 1292, 1216, 1173, 1084, 774 cm^{-1}; HRMS (ESI) calcd for $[C_{17}H_{21}NO_2Na]^+$ (M+Na$^+$) 294.1465; found 294.1463.

3.1.29 *N*-(4-Hydroxybutyl)-3,4-dimethoxybenzamide (**9**)

To a solution of 3,4-dimethoxybenzoic acid (547 mg, 3.00 mmol) and dimethylformamide (50 μL, 0.60 mmol) in dry toluene (10 mL) at 0 ℃ was added dropwise thionylchloride (0.24 mL, 3.30 mmol). The mixture was heated to 70 ℃ and stirred for 2 h. The reaction was then cooled to 0 ℃ and diluted with acetonitrile (15 mL). To the resulting mixture were added triethylamine (0.63 mL, 4.50 mmol) and 4-amino-1-butanol (268 mg, 3.00 mmol) at 0 ℃. The reaction mixture was warmed to room temperature and then heated under reflux for 12 h. The reaction was quenched with a saturated aqueous solution of $NaHCO_3$ and extracted with CH_2Cl_2 (40 mL×4). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel [*V*(EtOAc)∶*V*(*n*-hexane)=3∶1] to give compound **9** (698 mg, yield 92%) as a white solid, m.p. 92～93 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.60～1.66 (m, 2H), 1.66～1.73 (m, 2H), 2.87 (s, 1H), 3.44 (dd, *J*=12.4, 6.5 Hz, 2H), 3.67 (t, *J*=6.0 Hz, 2H), 3.87 (s, 3H), 3.88 (s, 3H), 6.81 (d, *J*=8.5 Hz, 1H), 6.93～7.00 (m, 1H), 7.31～7.35 (m, 1H), 7.41～7.44 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 26.2, 29.8, 39.8, 55.9 (2C), 62.1, 110.3, 110.6, 119.5, 127.2, 148.8, 151.6, 167.3; IR (film) ν_{max}: 3315, 3078, 2937, 2866, 1632, 1580, 1549, 1508, 1462, 1314, 1270, 1231, 1132, 1022, 879, 819 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_{19}NO_4Na]^+$ (M+Na$^+$) 276.1206; found 276.1203.

3.1.30 *N*-(4-Chlorobutyl)-3,4-dimethoxybenzamide (**4w**)

To a solution of **9** (1.013 g, 4.00 mmol) in mixture of toluene (53 mL) and chloroform (7.5 mL) at 0 ℃ was added thionylchloride (0.44 mL, 6.00 mmol) and the reaction was heated up to 60 ℃ for 2 h. The mixture was concentrated and the resulting residue was purified by flash chromatography on silica gel [*V*(EtOAc) ∶ *V*(*n*-hexane)=1 ∶ 2] to give compound **4w** (1.050 g, yield 97%) as a white solid, mp 93～95 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.72～1.80 (m, 2H), 1.81～1.89 (m, 2H), 3.43～3.49 (m, 2H), 3.57 (t, *J*=6.4 Hz, 2H), 3.89 (s, 3H), 3.90 (s, 3H), 6.52～6.58 (m, 1H), 6.84 (d, *J*=8.5 Hz, 1H), 7.30～7.33 (m, 1H), 7.42～7.44 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 27.0, 29.8, 39.2, 44.5, 55.9 (2C), 110.2, 110.5, 119.4, 127.1, 148.9, 151.6, 167.2; IR (film) ν_{max}: 3316, 3078, 2936, 2842, 1634, 1583, 1547, 1507, 1462, 1310, 1269, 1230, 1182, 1131, 1024, 868, 816 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_{18}ClNO_3Na]^+$ (M＋Na$^+$) 294.0867; found 294.0868.

3.1.31 *N*-(4-Bromobutyl)-3,4-dimethoxybenzamide (**4x**)

To a solution of **9** (633 mg, 2.50 mmol) in CH_2Cl_2 (7.5 mL) at 0 ℃ was added PBr_3 (330 mg, 1.20 mmol) and the reaction mixture was warmed to room temperature and stirred for 24 h. The reaction was quenched with a saturated aqueous solution of $NaHCO_3$ and extracted with CH_2Cl_2 (20 mL×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel [*V*(EtOAc) ∶ *V*(*n*-hexane)=1 ∶ 2] to give compound **4x** (525 mg, yield 68%) as a white solid, m.p. 93～94 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.72～1.82 (m, 2H), 1.88～2.00 (m, 2H), 3.40～3.52 (m, 4H), 3.90 (s, 3H), 3.91 (s, 3H), 6.40～6.52 (m, 1H), 6.84 (d, *J*=8.4 Hz, 1H), 7.26～7.34 (m, 1H), 7.40～7.45 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 28.3, 30.0, 33.3, 39.1, 56.0 (2C), 110.3, 110.6, 119.2, 127.1, 149.0, 151.7, 167.2; IR (film) ν_{max}: 3314, 2933, 2842, 1634, 1547, 1508, 1461, 1337, 1311, 1269, 1231, 1182, 1131, 1024, 871, 820, 764 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_{18}BrNO_3Na]^+$ (M＋Na$^+$) 338.0362; found 338.0367.

3.1.32 *N*-(4-Iodobutyl)-3,4-dimethoxybenzamide (**4y**)

To a cooled (0 ℃) solution of **9** (633 mg, 2.50 mmol) in THF (5.0 mL) was added PPh_3 (1.310 g, 5.00 mmol), imidazole (375 mg, 5.50 mmol) and I_2 (1.265 g, 5.00 mmol) sequentially. The reaction mixture was warmed to room temperature and stirred for 1 h. The reaction was quenched with saturated aqueous $Na_2S_2O_3$ (2 mL) and the layers were separated. The aqueous layer was extracted with EtOAc (20 mL×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel [*V*(EtOAc) ∶ *V*(*n*-hexane)=1 ∶ 2] to give compound **4y** (720 mg, yield 79%) as a white solid, m.p. 84～85 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.68～1.79 (m, 2H), 1.86～1.95 (m, 2H), 3.22 (t, *J*=6.8 Hz, 2H), 3.43～3.50 (m, 2H), 3.91 (s, 3H), 3.91 (s, 3H), 6.38～6.46 (m, 1H), 6.85 (d, *J*=8.4 Hz, 1H), 7.27～7.34 (m, 1H), 7.40～7.45 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 6.31, 30.6, 30.7, 38.9, 55.9 (2C), 110.2, 110.5, 119.3, 127.1, 148.9, 151.7, 167.2; IR (film) ν_{max}: 3310, 2922, 2850, 1633, 1580, 1543, 1506, 1460, 1309, 1268, 1229, 1178, 1131, 1023, 871, 819 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_{18}INO_3Na]^+$ (M＋Na$^+$) 386.0224; found 386.0219.

3.1.33 *N*-(4-Chlorobutyl)acetamide (**4z**)

To a solution of acetamide (177 mg, 3.00 mmol) in toluene (12.0 mL) at 0 ℃ was added 4-chloro-butyraldehyde (954 mg, 9.00 mmol) followed by triethylsilane (1.40 mL, 9.00 mmol) and trifluoroacetic acid (0.88 mL, 9.00 mmol) and the reaction was heated up to 80 ℃ for 12 h. The solvent was evaporated, the residue was dissolved in EtOAc and was washed successively with a saturated aqueous solution of $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel [*V*(EtOAc) ∶ *V*(*n*-hexane)=1 ∶ 1] to give compound **4z** (362 mg, yield 81%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 1.62～1.73 (m, 2H), 1.77～1.86 (m, 2H), 1.98 (s, 3H), 3.27 (dd, *J*=13.1, 6.8 Hz, 2H), 3.56 (t, *J*=6.5 Hz, 2H), 6.23 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 23.1, 26.8, 29.7, 38.7, 44.5, 170.3; IR (film) ν_{max}: 3293, 3085, 2935, 1653, 1554, 1440, 1370, 1259, 1172, 724 cm^{-1}; HRMS (ESI) calcd for $[C_6H_{12}ClNONa]^+$ (M＋Na$^+$) 172.0500; found 172.0509.

3.1.34 *N*-Butyl-4-formyl-2-methylbenzamide (**4aa**)

To a solution of 4-formyl-2-methylbenzoic acid (492 mg, 3.00 mmol) and dimethylformamide (50 μL, 0.60 mmol) in dry toluene (10 mL) at 0 ℃ was added dropwise thionylchloride (0.24 mL, 3.30 mmol). The mixture was heated to 70 ℃ and stirred for 2 h. The reaction was then cooled to 0 ℃ and diluted with CH_2Cl_2 (15 mL). To the resulting mixture were added triethylamine (0.63 mL, 4.50 mmol) and *n*-butylamine (219 mg, 3.00 mmol) at 0 ℃. The reaction mixture was warmed to room temperature and was stirred for 12 h. The reaction was quenched with 2.0 mL of 1.0 mol/L HCl and extracted with CH_2Cl_2 (40 mL×4). The combined organic layers were washed successively with a saturated aqueous solution of $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel [*V*(EtOAc) ∶ *V*(*n*-hexane)=1 ∶ 2] to give compound **4aa** (598 mg, yield 91%) as a white solid, m.p. 55～56 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 0.96 (t, *J*=7.3 Hz, 3H), 1.36～1.47 (m, 2H), 1.55～1.64 (m, 2H), 2.46 (s, 3H), 3.42 (dt, *J*=6.6, 6.6 Hz, 2H), 6.15 (s, 1H), 7.41～7.47 (m, 1H), 7.62～7.70 (m, 2H), 9.95 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 13.6, 19.4, 20.0, 31.6, 39.6, 127.0, 127.2 (2C), 131.8, 136.8, 142.3, 168.9, 191.7; IR (film) ν_{max}: 3279, 3075, 2960, 1697, 1643, 1607, 1543, 1465, 1383, 1296, 1228, 1108, 836, 776, 742, 671 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_{17}NO_2Na]^+$(M＋Na$^+$) 242.1151; found 242.1156.

3.1.35 4-(3,4-Dimethoxyphenyl)quinolizidin-2-one (**8**)

To a solution of **3y** (135 mg, 0.330 mmol) in toluene (10 mL) were sequentially added AIBN (160 mg, 0.980 mmol) and $(TMS)_3SiH$ (0.50 mL, 1.62 mmol). The resulting mixture was stirred at 75 ℃ for 1.5 h. After being cooled to r.t., the solvent was removed under vacuum. The residue was purified by flash column chromatography on silica gel [*V*(EtOAc) ∶ *V*(*n*-hexane) ∶ *V*(NH_3•H_2O)=1 ∶ 2 ∶ 0.05] to

give compound **8**[27i] (70 mg, yield 74%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.14～1.25 (m, 1H), 1.34～1.72 (m, 5H), 2.20 (dt, J=11.8, 3.3 Hz, 1H), 2.37 (ddd, J=15.0, 8.8, 1.3 Hz, 1H), 2.54～2.66 (m, 2H), 2.84～2.95 (m, 3H), 3.86 (s, 3H), 3.87 (s, 3H), 4.23 (dd, J=6.3, 4.0 Hz, 1H), 6.65～6.72 (m, 2H), 6.78～6.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 23.4, 24.0, 31.9, 46.8, 47.5, 51.3, 54.3, 55.8, 55.9, 63.9, 110.7, 111.8, 120.9, 131.6, 148.4, 148.7, 209.6; IR (film) ν_{max}: 3088, 2926, 2853, 1713, 1515, 1458, 1259, 1144, 1028, 810 cm^{-1}; HRMS (ESI) calcd for $[C_{17}H_{23}NO_3Na]^+$ (M+Na$^+$) 290.1756; found 290.1756.

3.1.36 (±)-Lasubine I (**5**)

To a solution of **8** (30 mg, 0.10 mmol) in THF (3 mL) at −78 ℃ was added dropwise a 1.0 mol/L solution of L-Selectride in THF (0.12 mL, 0.12 mmol). The mixture was stirred at −78 ℃ for 3 h and MeOH (0.15 mL) was added. The resulting suspension was treated with a 2.0 mol/L aqueous solution of NaOH (2.5 mL). The organic layer was separated and the aqueous phase was extracted with CH_2Cl_2 (10 mL×3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel [V(EtOAc)∶V(*n*-hexane)∶V(NH_3•H_2O) =1∶1∶0.02] to give (±)-lasubine I (**5**)[27i] (23 mg, yield 77%) as a colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.22～1.36 (m, 1H), 1.42～1.82 (m, 7H), 1.92～2.20 (m, 3H), 2.28～2.48 (m, 1H), 2.68～2.82 (m, 1H), 2.90～3.22 (m, 1H), 3.87 (s, 3H), 3.90 (s, 3H), 4.06～4.30 (m, 2 H), 6.78～7.10 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 23.9, 24.4, 32.2, 40.0 (2C), 51.0, 54.2, 55.8, 56.0, 61.7, 64.9, 110.7, 111.8, 120.6, 135.1, 148.0, 148.8; IR (film) ν_{max}: 3354, 2925, 2851, 1513, 1458, 1261, 1143, 1028, 956, 873, 805 cm^{-1}; HRMS (ESI) calcd for $[C_{17}H_{25}NO_3Na]^+$ (M+Na$^+$) 292.1907; found 292.1908.

3.1.37 1-(4-Iodobutyl)-2-methyl-2,3-dihydropyridin-4(1*H*)-one (**3ac**)

To a solution of chloride **3z** (54 mg, 0.25 mmol) in acetone (5.0 mL) was added NaI (375 mg, 2.50 mmol) and the resulting suspension was refluxed for 12 h. The reaction was cooled to room temperature, the solvent was evaporated under reduced pressure, and a 1∶1 mixture of Et_2O/H_2O (8.0 mL) was added. The organic layer was separated and the aqueous phase was extracted with CH_2Cl_2 (10 mL×3). The combined organic phase was washed with brine, dried over Na_2SO_4, filtered, and evaporated to afford **3ac** (71 mg, yield 97%) as a pale yellow oil, which was used without further purification in the next reaction step. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.25 (d, J=6.7 Hz, 3H), 1.70～1.80 (m, 2H), 1.82～1.94 (m, 2H), 2.24 (dd, J=16.3, 4.2 Hz 1H), 2.74 (dd, J=16.3, 6.7 Hz, 1H), 3.12～3.34 (m, 4H), 3.61～3.72 (m, 1H), 4.92 (d, J=7.4 Hz, 1H), 6.91 (d, J=7.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 5.5, 15.2, 30.1 (2C), 42.4, 52.0, 52.3, 97.0, 152.3, 190.5; IR (film) ν_{max}: 3052, 2923, 2853, 1574, 1460 cm^{-1}; HRMS (ESI) calcd for $[C_{10}H_{16}INONa]^+$(M+Na$^+$) 316.0169; found 316.0168.

3.1.38 (±)-Myrtine hydrochloride salt (**6**)

To a solution of **3ac** (30 mg, 0.10 mmol) in toluene (3.0 mL) were sequentially added AIBN (49 mg, 0.30 mmol) and $(TMS)_3SiH$ (0.16 mL, 0.50 mmol). The resulting mixture was stirred at 75 ℃ for 1.5 h. After cooling to r.t., the solvent was removed under vacuum. The residue was purified by flash column chromatography on silica gel [V(EtOAc)∶V(*n*-hexane)∶V(NH_3•H_2O)=1∶2∶0.05] and 1.0 mL of 1.0 mol/L HCl was added to give (±)-myrtine (**6**) hydrochloride salt (16 mg, yield 78%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.30 (d, J=5.9 Hz, 3H), 1.38～1.50 (m, 1H), 1.88～2.04 (m, 3H), 2.26～2.43 (m, 2H), 2.42～2.60 (m, 2H), 2.82～2.96 (m, 1H), 3.11～3.21 (m, 1H), 3.23～3.34 (m, 1H), 3.40～3.51 (m, 1H), 3.92～4.10 (m, 2H), 12.85 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 12.7, 21.8, 22.7, 30.6, 45.1, 45.7, 52.4, 56.6, 58.9, 201.6; IR (film) ν_{max}: 3317, 2922, 2852, 1733, 1459, 1268, 1100, 770 cm^{-1}; HRMS (ESI) calcd for $[C_{10}H_{18}NO]^+$ (M−Cl)$^+$ 168.1383; found 168.1385.

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